

Please replace the second paragraph on page 9 with the following paragraph:

A<sup>1</sup>  
In the sitting drop configuration 130, a drop 132 of crystallization solution is placed in a receptacle on the top of an upstanding column 126 where conditions lead to supersaturation in the drop 132 and the initiation of precipitation which forms a crystal 108.

Please replace the second paragraph on page 12 with the following paragraph:

A<sup>2</sup>  
In a preferred embodiment, a beam-stop 127 is provided between the incubator 102 and the X-ray detector 116 to stop a central non-diffracted X-ray beam from damaging the detector or adversely affecting the results. The spot size of the X-ray beam 120 at the detector (or beam stop) is preferably about 40 to 50 microns in diameter, with a divergence of no greater than 30 arc-seconds. A means for inserting a calibration crystal into the X-ray beam, is also preferably provided to calibrate the apparatus 100.

Please replace the paragraph starting on page 14, line 16 and ending on page 15, line 8 with the following paragraph:

A<sup>3</sup>  
**Figure 4** is a flow chart of a method of screening for crystals according to an embodiment of the invention. The incubator 102 (**Figure 1**) is preferably first placed (step 402) onto the positioner 300 (**Figure 3**). The incubator 102 can conveniently be placed with a "pick and place" robot arm known to those of skill in the art. The imaging system 202 (**Figure 2**) is then preferably activated (step 404) and moved over the incubator. Alternatively, the positioner can move the incubator relative to the imaging system. The activation (step 404) of the imaging system entails scanning each well 122 to determine (step 418) the presence and/or location (step 416) of a potential crystal. The imaging system 202, therefore, scans each well of the incubator for potential crystal material such as single crystals and microcrystals. The location of each visually acceptable potential crystal is then preferably stored (step 406) by the imaging system. The imaging system is then retracted from its scanning position adjacent to the incubator. Using the stored location of

A3

each potential crystal, the positioner moves the incubator 102 or the X-ray detector 116 to align or position (step 408) each potential crystal with a line coincident with the emitted X-ray beam. Each located potential crystal is then irradiated (step 410) by the X-ray beam 120 (Figure 1) emitted from the X-ray source 114 (Figure 1). The X-ray detector 116 (Figure 1) detects (step 412) any diffraction from the irradiated crystal, whereafter the detected diffraction patterns are stored and/or analyzed. The positioner can optionally locate the next potential crystal (step 414) and the process can be optionally repeated until all detected crystals have been irradiated and their diffraction patterns stored and/or analyzed, where the diffraction pattern indicates the presence of one or more well ordered crystal. The overall time to assess the quality of diffraction of a single crystal is approximately 5 minutes.

---

Please replace the final paragraph on page 16 with the following paragraph:

---

A4

All exposures led to a diffraction pattern that had a band of diffuse scattering 602 (Figure 6) which was centered around 4 - 5 Å resolution. This 4 - 5 Å band was probably due to diffraction from paraffin oil. On several, but not all, exposures, a second scattering ring centered around 8Å appeared. Since this second band appeared at exposures corresponding to approximately 2.5 mm translations of the plate, this ring was probably due to scattering from the walls of the wells of the plate which are spaced 2.25 mm apart. Some samples yielded no X-ray diffraction indicating that the X-ray beam did not pass through crystalline material. However, when the X-ray beam passed through some of the samples of lysozyme, intense diffraction patterns were observed indicating the presence of well-ordered crystals in the samples. Further exposures showed that one could observe diffraction out to 1.8Å from the lysozyme crystal *in-situ*. Examples of diffraction of the crystal are referenced by numeral 606. It can also be observed that no diffraction occurs at the center 604 of the image due to placement of the beam stop 127 (Figure 1).

---